REMARKS

Claims 1, and 3-13 are pending in the application. The same are presented for examination upon entry of the present amendment. Claim 1 is independent. Claim 2 is canceled without prejudice.

Claim rejections, 35 U.S.C. § 112

The Office Action rejects claim 7 under 35 U.S.C. §112, ¶1, alleging that the subject matter of the claim is not enablingly described in the Specification. Applicants respectfully traverse.

The vectors of claim 7, pBCKI I, pBCKI II, pBCKIDT I, and pBCKIDT II, are clearly described as illustrated in Figs. 1, 2, 3, and 16, and the method for producing them is completely and precisely described in the detailed description and figures of the present application to the extent that those skilled in the art can easily produce and use them.

Specifically, example 1 and the figures relating to example 1 describe, in detail, a material vector for producing the vectors of claim 7, means for obtaining the material vector, restriction enzymes being used, and primers being used, and the process for producing the vectors, pBCKI I, pBCKI II, pBCKIDT I, and pBCKIDT II, from the material vector, is clearly explained in detail using the figures. Those skilled in the art appreciate that vectors can be produced through cleaving and connecting said constituents and frames, using in order the restriction enzymes predetermined from the material vectors comprising each of their constituents and frames. Therefore, referring to the detailed description and figures of the present application, those skilled in the art can easily produce the vectors, pBCKI 1, pBCKI II, pBCKIDT 1, and pBCKIDTII, without undue trial and error.

The Office Action rejects claims 10-13 under 35 U.S.C. §112, ¶1, arguing that claims that are not specific to a donor cell type are not enabled by description directed to bovine donor fibroblasts and enucleated bovine oocytes.

The method of present claim 10 now recites that the introduction of the bovine beta-casein gene-targeting vector is into a bovine embryonic cell or fibroblast cell. This, as the Office Action correctly recognizes, is enabled by the Specification. Applicants submit that claim 10 as presently amended overcomes the Office Action's §112¶1 rejection. Applicants submit that claim 11, by virtue at least of its dependence from claim 10, is proper under §112¶1.

Present claim 12, in like fashion to claim 10, now specifies a step of introducing a vector into a bovine embryonic cell or fibroblast cell. Present claim 12 further elaborates that the nucleus of the bovine gene targeting cell is introduced into an enucleated bovine oocyte to produce a nuclear-transferred bovine embryo. Present claim 12 does not recite inter-species nuclear transfer. Applicants submit that present claim 12 overcomes the Office Action's §112¶1 rejection. Applicants submit also that claim 13, by virtue at least of its dependence from claim 12, is proper under §112¶1.

The Office Action rejects claims 8 and 9 under §112 ¶2. The Office Action argues that claims 8 and 9 are confusing as to the location of the somatic cell and embryo; and that it is unclear whether the cell or embryo is an intact bovine.

Present claim 8 is now recites that the isolated bovine somatic cell is produced by introducing the vector of claim 1 or 5 into an isolated bovine somatic cell and permitting the insertion of the DNA construct of the vector into the endogenous beta-casein gene by homologous recombination. Present claim 9 now clarifies that an isolated bovine embryo is produced by introducing the nucleus of the bovine somatic cell of claim 8 into an enucleated bovine oocyte to produce a bovine embryo.

Claim rejections, 35 U.S.C.§ 103

The Office Action rejects claims 1-6 under §103(a) as being unpatentable over Bonsing et al., Australian J. Biol. Sci., 1988, Vol. 41(4), pp. 527-537; Shen, et al., Chinese J. Biotechnol., May 2004, Vol. 20(3), pp. 361-365; and U.S. Patent 5,843,705 of DeTullio, et al.

Present claim 1 now specifies that the first region has a length of about 6 kb. Support for this feature is found in FIGS. 2 and 3. The expression "about" has been added because, Applicants submit, a small error from 6 kb, namely 6000 bases, is not in the range which can be identified through an experiment in the field of biotechnology. The length and position of the first region and the second region are elements critical to gene targeting efficiency.

The combination of Bonsing, Shen, and DeTullio does not disclose claim 1. Particularly, in reference to the present application at page 26, line 15 through page 27, line 23 of the Specification, and the English abstract of Shen at lines 7-11, the distinctions are shown below.

	Present Disclosure	Shen
Position of a second region	Comprises exons 5 to 8	Comprises exons 8 to 9
Position of a positive selection marker	Corresponds to introns 2 to 4 (to minimize the positional interference when homologous recombination events occur).	Corresponds to intron 7
Whether a cloning site exists behind a first region	As a foreign gene is inserted into the cloning site behind a first region, a gene targeting vector having the foreign gene inserted has *two* homologous regions.	As a foreign gene is sub-cloned at the position of exon 2 in a first region, a gene targeting vector having the foreign gene inserted has *three* homologous versions.

Due to the differences as above summarized, the gene targeting vectors prepared according to the present invention and Shen differ in their targeting efficiencies (*see* page 47, lines 4-9 of the present invention).

Specifically, in the case of introducing the vectors of the present invention, pBCTPOKI II and pBCTPOKIDT II having a TPO gene inserted into a bovine EF cell, their gene targeting efficiencies show 18.2% (10/55) and 41.4% (12/29), respectively. This is in contrast with 12.7% (31/244), the gene targeting efficiency in the case of introducing the vector of D2, pGBC4tPA, into a goat EF cell, by which it can be seen that they have remarkably high efficiencies. *See* Table 2 of the specification of the present application; Table 1 of Shen.) The difference in their efficiencies as above results from the length and positions of the regions of claim 1.

Bonsing discloses only the genomic organization of the bovine ß-casein gene, and fails to disclose claim 1. In addition, DeTullio does not disclose the length and position of a second region or a positive selection marker, as required by claim 1. Further, DeTullio does not disclose or suggest the vector cassette of the present invention.

The cited combination of art does not disclose claim 1. Applicants submit that the excellent targeting efficiency achievable with the present invention results the features of claim 1, and the claimed invention is not anticipated or rendered obvious by the cited combination of art. Applicants are respectfully requesting that the §103 rejection of claim 1 be reconsidered and withdrawn.

Claims 2-6, by virtue at least of their dependence from claim 1, are also patentable over the cited combination of art. Applicants likewise are requesting that the §103 rejections of claims 2-6 be reconsidered and withdrawn, and that claims 2-6 be passed to allowance.

The Office Action rejects claims 8-13 as it does claims 1-6, further in view of U.S. pre-grant publication 20050177878 of Melo, et al.

Melo is introduced by the Office Action for the proposition of producing transgenic cattle by nuclear transfer using a bovine fibroblast donor cel, where the firbroblast contains a DNA construct comprising a beta-casein 5' promoter operably linked to HGH.

However, Melo, either alone or in the cited combination with Bonsing, Shen, and DeTullio, does not disclose claim 1, from which claims 8-13 depend. By virtue at least of this dependence, claims 8-13 define patentably over the cited combination of art. Reconsideration and withdrawal of the §103 rejection of claims 8-13, and passage of claims 8-13 to allowance, are earnestly solicited.

To advance the prosecution, the Examiner is invited to contact the undersigned attorney.

Respectfully submitted,

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